UPWARD

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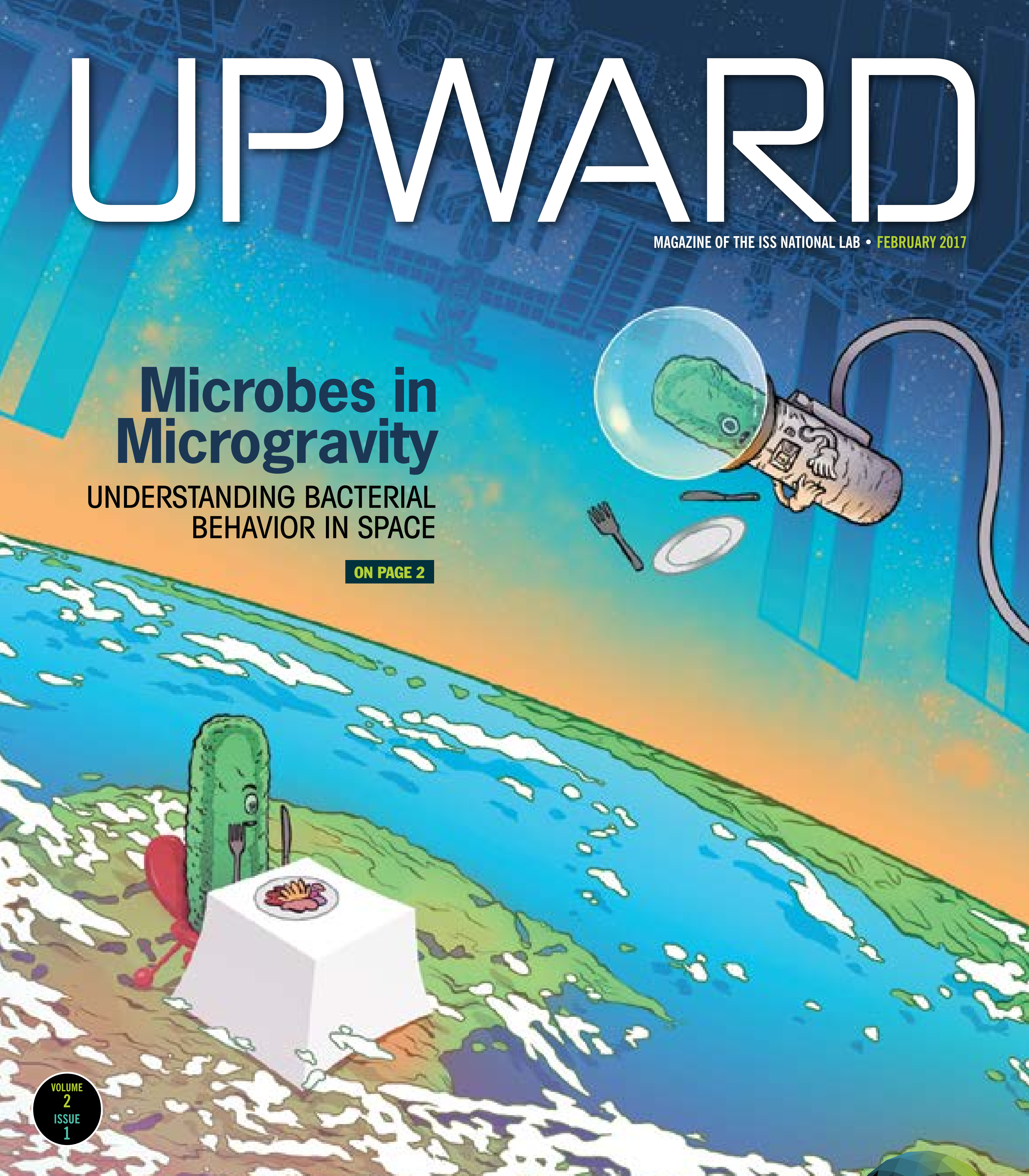

Microbes in Microgravity

UNDERSTANDING BACTERIAL BEHAVIOR IN SPACE

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VOLUME 2 ISSUE 1

CASIS™

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THE VIEW FROM THE CUPOLA

BY GREGORY H. JOHNSON, CASIS

Former Astronaut Gregory H. Johnson is the President and Executive Director of CASIS

After the completion of another record year, the ISS U.S. National Laboratory continues to expand the frontiers of science in low Earth orbit! In 2016, we saw Astronaut Kate Rubins observe, for the first time ever, heart muscle cells beating in orbit: one of several groundbreaking stem cell investigations in space. A diverse portfolio of payloads—58 in total—were launched to the ISS National Lab. These payloads were rich in discovery science, new technologies, and enabling platforms, powered by a growing community of new and returning researchers. Strong investment interest in the ISS National Lab from non-NASA sources grew, including universities, other government agencies, and the commercial sector.

The ISS National Lab mission is exciting and meaningful to everyone on Earth—serving our national interest to maximize the value of this one-of-a-kind asset, to increase access to new users, and to help accelerate the growth of our commercial economy in space. I could not be prouder of the ISS National Lab team, composed of dedicated professionals from NASA, CASIS, implementation partners, launch providers, and a broad community of users.

One year ago, we launched the first issue of *Upward*, and now we begin our second volume with articles highlighting an interesting cross section of recent in-orbit activities. Kudos to our entire scientific writing team—with articles from multiple contributors—who have built and grown this informative magazine for the ISS National Lab community.

Within this issue, you can learn about cutting-edge research in bacterial gene expression and cell behavior in space. We continue to observe and discover new phenomena in the unique ISS environment, where the effects of gravity on living and non-living systems alike can be isolated in ways not possible on Earth. It's amazing to me—the breadth and depth of research now being performed on the Space Station. Of course, ISS National Lab investigators not only take advantage of the continuous microgravity environment, but also utilize the vantage point of our world's only manned satellite. In this issue, we highlight three "outward" facing projects: a project examining meteors traveling through the Earth's atmosphere to probe what our early solar system was like, an investigation to test an innovative charge injection device to directly image distant Earth-like planets in other solar systems, and the Alpha Magnetic Spectrometer—a state-of-the-art in-orbit particle detector pointed at our heavens to better understand our universe.

Looking forward, there is much work to do in 2017. The space community is in a transition year, and we will see new faces in key government leadership positions. Our nation will continue to innovate, inspire, and challenge the status quo with new ideas. We'll see business-to-business R&D opportunities flourish, which will lead us to new markets for products and services and novel discoveries, all enabled by space-based research for use on Earth. We will see companies and institutions new to space launching their first projects into space. Additionally, we expect ISS educational and inspirational opportunities to multiply, as science, technology, engineering, and mathematics programs and partnerships mature and generate new outreach channels. The fascinating results of ISS National Lab research will continue to be revealed and will stretch our minds with new data, tools, and knowledge.

The payback from the ISS National Lab to life on Earth is a gift to our nation and to the world, with great promise for what lies ahead. While I've enjoyed many incredible vantage points in my 30-year career in aerospace—from different perspectives on the ground, in the air, and onboard the ISS—the view right now is the one that leaves me the most inspired about our future. ■

MICROBES IN MICROGRAVITY:

ANALYZING GENE EXPRESSION TO BETTER UNDERSTAND BACTERIAL BEHAVIOR IN SPACE

BY AMELIA WILLIAMSON SMITH

NASA Astronaut Rick Mastracchio using a crank to activate a group activation pack (GAP) onboard the ISS for the AES-1 experiment.
NASA

By observing the health of astronauts that travel into space, scientists have learned that microgravity has important effects on the human body, causing substantial changes to our bones and muscles. However, scientists have also found that microgravity has dramatic effects on far smaller living organisms, such as bacteria.

Bacteria behave differently in the microgravity environment of space than they do in a 1-g ground environment. For example, scientists have observed that in space, some strains of bacteria appear to exhibit enhanced growth and increased virulence (ability to cause disease). Additionally, higher doses of antibiotics are needed to kill some bacteria in space.

Scientists believe that these behavioral changes are not necessarily a direct effect of microgravity acting on the bacteria themselves—so what causes these changes in bacterial behavior?

ALTERING THE ENVIRONMENT AROUND BACTERIA

One model—the altered extracellular environment model—hypothesizes that the changes in bacterial behavior are actually an indirect effect of the microgravity environment, said Luis Zea, a researcher at BioServe Space Technologies at the University of Colorado, Boulder. The model postulates that microgravity alters the immediate environment around the bacterial cells, which then leads to changes in bacterial behavior.

"On Earth, there are different flows and forces, such as sedimentation, buoyancy, and convection, that don't exist in space because they are gravity dependent," Zea said. "The model states that it is the lack of these forces and flows that creates a different environment around the bacteria."

Dr. Luis Zea preparing the AES-1 experiment at Kennedy Space Center prior to the launch of Orbital ATK CRS-1.
BioServe Space Technologies

Zea and his team conducted an experiment called Antibiotic Effectiveness in Space-1 (AES-1), in which they compared gene expression data from a nonpathogenic (not disease-causing) strain of *Escherichia coli* bacteria grown onboard the ISS National Lab with cultures grown on the ground. AES-1 was launched to the ISS on Orbital ATK CRS-1 and returned to Earth on SpaceX CRS-3 and SpaceX CRS-4. Results from AES-1—published in the journal *PLoS ONE* in November 2016—strongly support the altered extracellular environment model.

"Through AES-1, we were able to corroborate, for the first time, this altered extracellular environment model that has been hypothesized for decades and could not be proven empirically or computationally," Zea said. Although the AES-1 data only shows correlation and not yet causation, the results shed light on why bacteria behave the way they do in microgravity and open the door to further research on unicellular organisms.

PEEKING INSIDE BACTERIAL CELLS

On Earth, the movement of bacterial cells through their media is influenced by the physical properties of the medium, including gravity-driven forces like buoyancy and sedimentation, as well as other forces, such as the viscosity of the medium. As the cells move, they interact with fresh media and absorb molecules of nutrients. The cells also excrete waste products that may sediment down, float up, or trail behind the cells if they move, while simultaneously diffusing away.

However, in microgravity, these gravity-driven forces are absent, and the transportation of nutrients to cells and waste products away from cells are limited to diffusion-only transport. The altered extracellular environment model hypothesizes that the resulting reduction in the movement of molecules leads to less interaction of the cells with fresh media and thus reduced availability of nutrient molecules for absorption. Additionally, less movement causes waste products to accumulate around the cells, resulting in higher concentrations of potentially toxic compounds. The model postulates that these changes in the immediate environment around the cells are what lead, at least in part, to the changes in bacterial behavior observed in microgravity.

Researchers had tried to confirm the altered extracellular environment model using both physical measurement techniques and computational modeling; however, both methods fell short. Gene expression analysis gave researchers a new way to look at bacteria and test the model. If the model is correct, one would expect to see specific differences in gene expression in the bacteria grown in space versus ground controls, said AES-1 principal investigator David Klaus, professor at the University of Colorado, Boulder and faculty affiliate of BioServe Space Technologies.

> *"The gene expression data gives us a little peek inside the cell, which we have not had before," Klaus said. "It is another layer that we've peeled back as we continue to try to figure out how bacteria respond to microgravity."*

HANDLING TEST TUBES IN SPACE

For the AES-1 experiment, the research team prepared 128 bacterial culture samples to send to the ISS National Lab. The samples were each contained in a fluid processing apparatus (FPA), a test tube specially designed by BioServe Space Technologies for use in microgravity. Each FPA has four separate chambers—the first containing the growth medium with nutrients (glucose molecules), the second containing the *E. coli* bacteria, the third containing an antibiotic, and the fourth containing a fixative to preserve the sample for analysis back on the ground. Two different antibiotics were each tested under 16 conditions (different drug concentrations and fixatives), and all were tested in quadruplicate.

BioServe Space Technologies

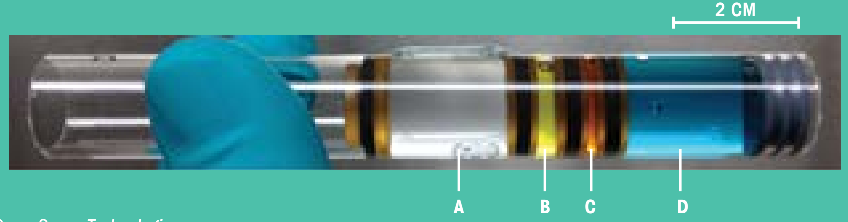
BioServe Space Technologies

Groups of eight FPAs were loaded into 16 BioServe Space Technologies group activation packs (GAP), which are cylinders that hold the FPAs and control the release of the solutions from the different compartments. Once the samples were onboard the ISS, a crew member used a crank to rotate the top of each GAP, introducing the bacteria in each FPA into the growth medium to start the experiment. The bacteria were left to grow, and then the antibiotics of varying concentrations were introduced into the samples using the GAP.

> *"In space, you can't just take test tubes and transfer the contents from one to another," Klaus said. "The BioServe Space Technologies hardware allows us to first isolate the fluids and then sequentially mix them to start and stop the experiment within a single container without introducing the possibility of fluid leakage in the cabin."*

Once the AES-1 flight samples were returned to Earth, the research team performed gene expression analysis on the flight samples and ground controls at the HudsonAlpha Institute for Biotechnology in Huntsville, Alabama. This allowed the research team to examine—at a molecular level—the responses of the bacterial cells to their environment. The team compared the gene expression data from the microgravity-grown bacteria to the ground controls to determine if the flight results matched those predicted by the altered extracellular environment model.

BIOSERVE'S FLUID PROCESSING APPARATUS (FPA)



A: 2.75 mL of sterile growth medium with glucose

B: 0.50 mL of *E. Coli* bacteria in minimal medium without glucose

C: 0.25 mL of antibiotic solution

D: 2.10 mL of fixative

BioServe Space Technologies

CORRELATING OBSERVATIONS WITH THE MODEL

If the model is correct, the microgravity-grown bacterial cells would have reduced interaction with fresh media and thus less nutrients available (even though the same amount of nutrients was provided for the flight samples and ground controls). Therefore, the researchers expected to see signs that the bacterial cells grown in microgravity were experiencing starvation conditions—and, indeed, they did.

The researchers found an overexpression of genes in the microgravity-grown cells, relative to the ground controls, that indicate the cells grown in space experienced a lack of available nutrients. They also observed an overexpression of genes associated with the metabolism of other carbon sources (non-glucose nutrient molecules) that were not present in the growth medium. "It is believed bacteria do this to be able to change their metabolic pathways as soon as another carbon source becomes available," Zea said. "This can be compared to the risk-prone foraging strategy that some animals use, in which they start engaging in high-risk behaviors looking for food."

Analysis of the microgravity-grown bacteria also revealed an overexpression of genes associated with the metabolism of glucose, which may explain why some types of bacteria exhibit enhanced growth in space. Related to this, the team also found an increased expression of genes associated with acid production—acetic acid is a waste product of glucose metabolism.

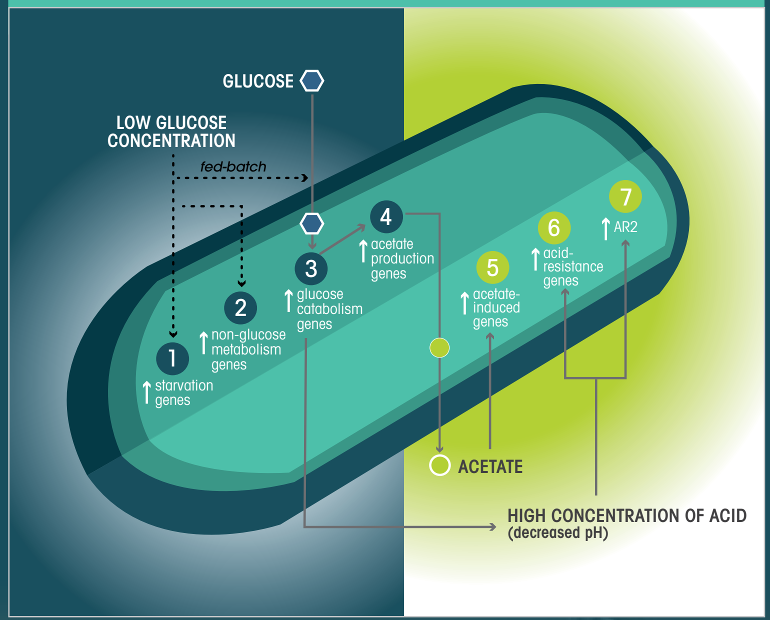
It may seem counterintuitive that there was an increase in cell growth, given that the cells were under starvation conditions; however, this same phenomenon has been observed to happen on Earth under a very specific growth condition called fed-batch processing, Zea said. Scientists have found that higher bacterial cell counts occur when nutrients are absorbed incrementally (such as under starvation conditions), as opposed to when there is a steady absorption of nutrients (under normal batch conditions).

If the altered extracellular environment model is correct, the researchers also expected to see signs of higher concentrations of waste products, such as acetic acid, around the microgravity-grown cells due to the reduced mass transport of chemical compounds around the cells—and, again, they did.

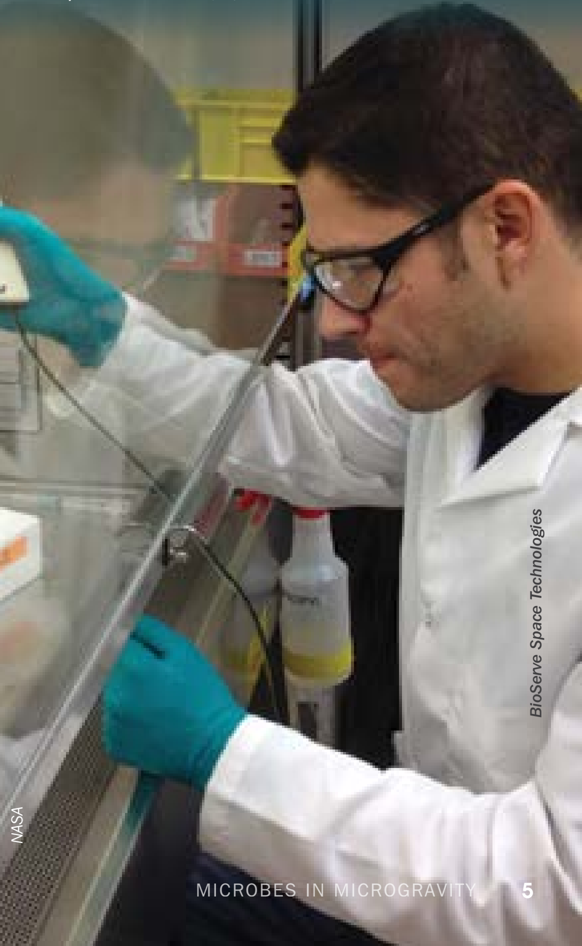
ALTERED EXTRACELLULAR ENVIRONMENT MODEL

Blue circles represent the overexpression of genes associated with metabolism.

Green circles represent the overexpression of genes associated with acidic environment conditions.



Zea L, Prasad N, Levy SE, Stodieck L, Jones A, Shrestha S, et al. (2016) A Molecular Genetic Basis Explaining Altered Bacterial Behavior in Space. PLoS ONE 11(11): e0164359.



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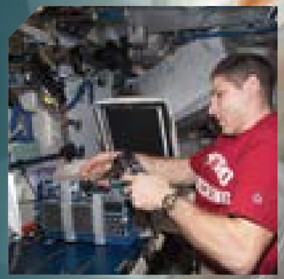


NASA

In the microgravity-grown bacteria, the team found an overexpression of genes associated with acid resistance, suggesting increased acidity in the environment around the cells. However, the team did not observe differences in acidity of the bulk fluid around the cells in microgravity versus ground controls, suggesting the acidic environment in microgravity is limited to the immediate area around the cells. The buildup of acid may also explain the observed increase in virulence of some bacteria in space, as researchers have seen a correlation between an increase in acidity and an increase in virulence in certain bacterial strains, Zea said.

Together, these results provide strong support for the altered extracellular environment model. "I think the gene expression data was a real breakthrough," Klaus said, "but it doesn't prove cause and effect; it only shows correlation. Moving forward, we can begin to ask more definitive questions to get a much better understanding of what's going on."

Additional research is needed to confirm why higher concentrations of antibiotics are needed to kill bacteria in space. However, the altered extracellular environment model suggests that it may not be that bacteria have increased resistance to antibiotics in space, but instead, encounter less antibiotic due to the reduced concentration of antibiotic drug molecules around the cells.

NASA

"We're trying to differentiate between bacterial drug resistance and bacterial susceptibility to drugs," Zea said. "Is it that fewer drug molecules are reaching the cell due to the altered extracellular environment, thus physically reducing susceptibility, or is it that the cells are turning on resistance mechanisms more effectively? Or, it could be a mixture of the two, or something else altogether—that question is still open."

ADVANCING KNOWLEDGE OF CELLS IN SPACE

The microgravity environment on the ISS National Lab allows researchers to probe the interactions between bacterial cells and their environment, and the resulting influences on bacterial behavior, in unique ways. "We're trying to understand what's going on at the interface of a cell and its environment," Klaus said. "And in the absence of gravity, you can tease out some of these relationships in ways that are not really possible to recreate on Earth."

Understanding changes in bacterial behavior in space is important not only because it helps better protect astronauts from infection during future long-duration spaceflight missions, but it also illuminates the mechanisms of bacterial behavior in our bodies on Earth. Additionally, an understanding of the mechanisms by which the altered extracellular environment in space triggers behavioral changes in microorganisms and our own cells informs research aimed at developing new vaccines, uncovering novel molecular targets against drug-resistant bacteria, and developing new antibiotics.

"There's always an interplay between basic research and applied research, and they build on each other," Klaus said. "So the more we understand the fundamental mechanisms, the more we can then use that knowledge to go after the real end goal—the development of application-oriented products." ■

MAKING BACTERIA SELF-DESTRUCT

While analyzing the AES-1 gene expression data, the research team found something interesting about the genes that enable bacterial cells to self-destruct.

It is believed bacteria self-destruct under certain types of stress to ensure the survival of the colony. Scientists have long wondered if this mechanism could be exploited to kill bacteria that have become resistant to antibiotics by activating the genes that control self-destruction, often called "suicide" genes.

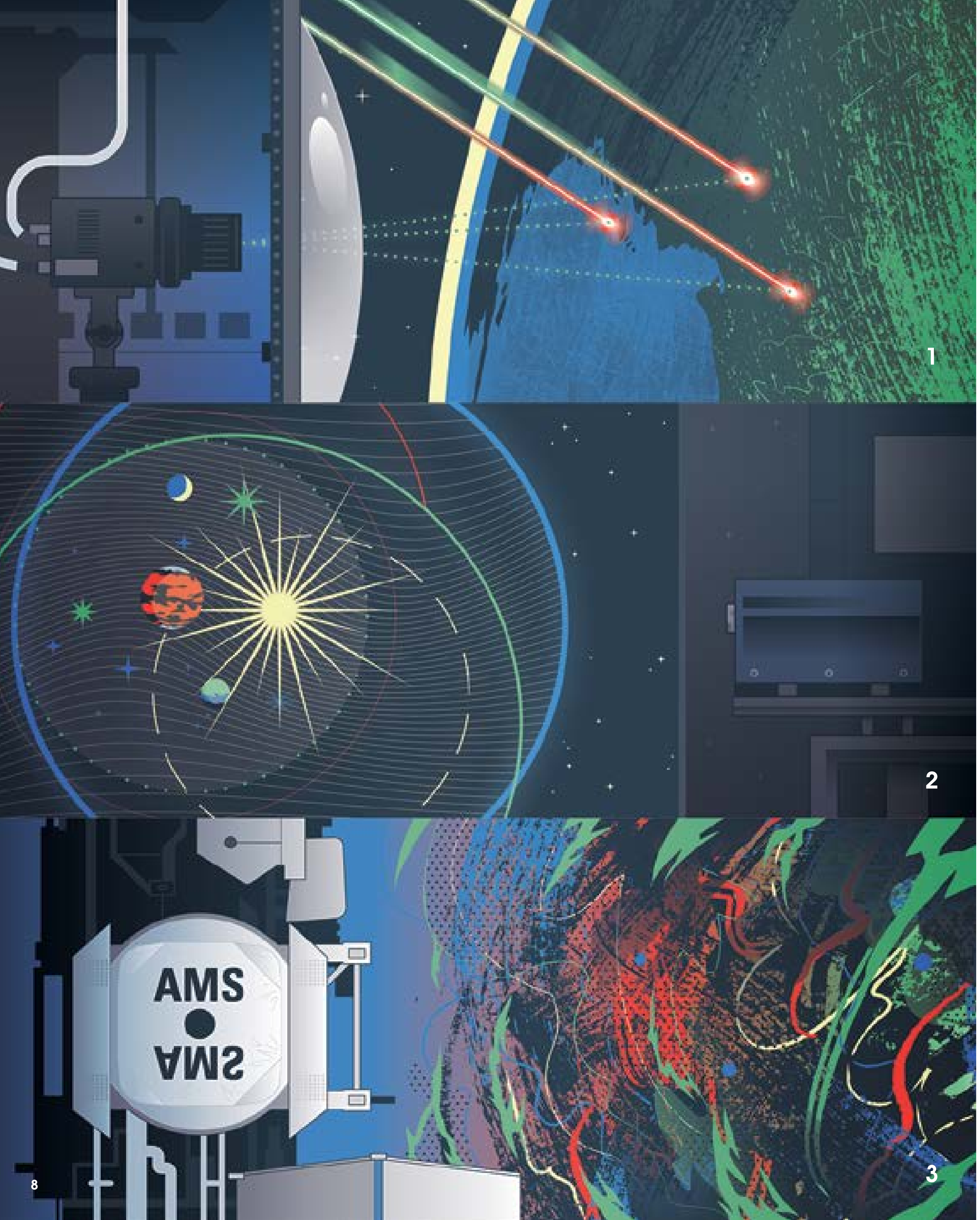
"The problem is that if you turn on the known activator for the suicide genes, then you're also activating 156 other genes that actually make the bacteria worse," Zea said.

The suicide genes are actually a pair of genes—one is a toxin, which triggers self-destruction, and the other is an antidote, which keeps the toxin gene under regulation. The AES-1 data showed a 24-fold increase in the expression of the toxin gene and a 40-fold underexpression of the antidote gene in one of the 16 tested conditions. And the interesting part, Zea said, is that the known activator for the genes was not turned on—which means that perhaps there is a second unknown activator.

"In space, the antidote gene was turned off and the toxin gene was overexpressed by 24 times, which is rather remarkable," Zea said. "Those out-of-the-roof numbers combined with the fact that the known activator was not differentially expressed indicates that there may be another activator that we could look into as a potential target for novel drugs."

For AES-1, each condition was tested in quadruplicate in microgravity and in ground controls. The research team found this overexpression of the toxin gene and underexpression of the antidote gene in all four microgravity replicates of the tested condition, but not in any of the ground samples.

An indication of a possible second activator has never before been observed, and the team hopes to probe this further in future microgravity research. If a novel activator is discovered, it could eventually lead to the development of a new class of antibiotics.



ON THE FRONTIER OF SPACE: LOOKING OUTWARD

TO BETTER UNDERSTAND THE UNIVERSE AROUND US

BY AMELIA WILLIAMSON SMITH

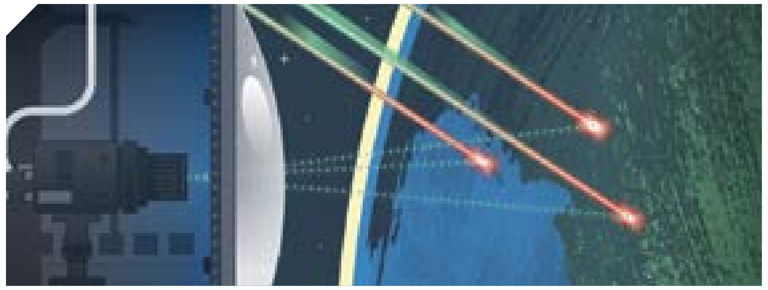
The ISS National Lab is an outpost on the frontier of space. It is a point from which we can peer out into the undiscovered vastness of the universe to discover who we are, how we got here, and where we are going. From this outpost for observation and innovation in space, it is possible to conduct research off of Earth for the benefit of life on Earth.

The research on the ISS is diverse and spans many fields—including rodent research aimed at elucidating the mechanisms behind disease; protein crystallization seeking to improve drug design; understanding gravity's effects on plant growth to enhance crops on Earth; testing materials and technologies in space to improve products on the ground; and studies of our planet, its ecosystems, and climate from the vantage point of low Earth orbit.

But not all research on the ISS is focused on Earth—some researchers have turned their gaze outward and are utilizing the ISS National Lab to gain a better understanding of the universe around us.

Three such outward-looking projects include:

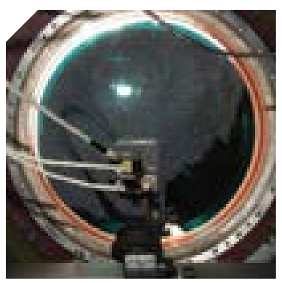
1. **Project Meteor**, which is examining meteors as they burn through Earth's atmosphere to learn more about asteroids and comets—some of the oldest bodies in our solar system.
2. A project to test a new type of technology called a **charge injection device** that can be used to directly image exoplanets (planets outside our solar system) around distant stars.
3. The **Alpha Magnetic Spectrometer-02 (AMS-02)** project, an international collaboration searching for evidence of dark matter and primordial antimatter to better understand the origin and composition of our universe.



STUDYING METEORS TO UNCOVER CLUES ABOUT THE EARLY SOLAR SYSTEM

For thousands of years, humans have looked up in awe at the beauty of meteors streaking brightly across the night sky. Now, from the vantage point of the ISS, researchers are able look at meteors in a new way—they can look down and observe meteors from above as they enter Earth's atmosphere.

Project Meteor, which launched on Orbital ATK CRS-6 in March 2016, will spend two years collecting images of meteors crossing the Earth's atmosphere using a high-definition camera positioned in the Window Observational Research Facility (WORF) in the Destiny module of the ISS. The project is a collaboration between researchers at the Southwest Research Institute in San Antonio and Japan's Planetary Exploration Research Center at the Chiba Institute of Technology.



NASA

By analyzing these images, researchers can obtain information about the physical and chemical properties of meteoroids (rock and dust particles from space that enter Earth's atmosphere), such as their size, density, and chemical composition. Most meteoroids come from known comets and asteroids. By studying the rock particles as they burn through the atmosphere, scientists can learn more about these parent bodies, said project Meteor payload developer Michael Fortenberry, principal engineer at the Southwest Research Institute.

"In essence, meteors are just little pieces of dust and rock that are entering the atmosphere and burning up, which is what you see from the ground," Fortenberry said. "But ultimately, that dust and rock is coming from something else far out in the solar system that has been traveling around the sun for millions of years, and we're basically getting to catch a little piece of it as it comes to the Earth."

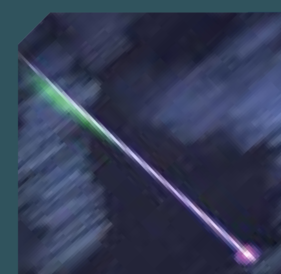
Comets and asteroids are some of the oldest objects in our solar system. By studying their composition and properties, scientists get a glimpse of what the early solar system was like before the planets formed, which helps them better understand the origin of our solar system, Fortenberry said. "There have been several space missions out to comets and asteroids, but this is a way of doing it a little closer to Earth and a lot cheaper."

The biggest advantage of observing meteors from space is being above Earth's atmosphere and atmospheric elements such as clouds, which block the view, Fortenberry said. Ground observations of meteors are also limited to short periods of time and small portions of the atmosphere.

Project Meteor will allow researchers to monitor meteors passing through Earth's atmosphere over longer periods of time without the limitations of atmospheric interference.

The project Meteor camera records continuous video during each night pass as the ISS orbits the Earth. The camera's lens is designed with a wide aperture, allowing it to capture high-resolution images in low light that enable the detection of even small meteors.

The project is already generating large amounts of data, currently filling a 750-GB hard drive each week. The team has received some of the data for analysis by downlink, but for the rest they must wait until the hard drives return to Earth on SpaceX CRS-10, which launched to the ISS earlier this month.



Composite image of a meteor taken by the project Meteor camera during the Perseid meteor in November 2016.

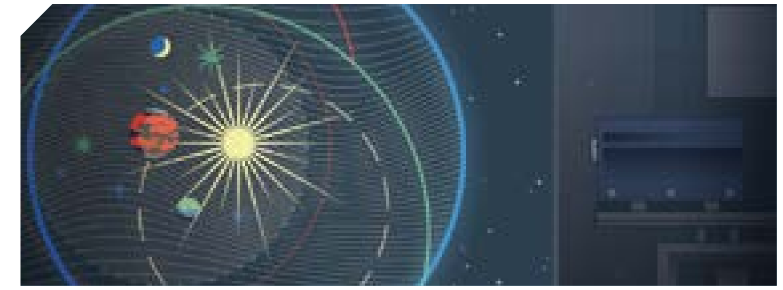
Project Meteor

ANALYZING THE CHEMICAL COMPOSITION OF METEORS

The project Meteor camera is equipped with a diffraction grating, a piece of glass etched with a series of prisms that diffracts incoming light into different wavelengths, enabling spectral analysis to determine the chemical composition of the meteors.

As meteors enter the atmosphere, they burn at different temperatures, depending on the specific elements in the meteoroid. When the elements burn at different temperatures, they emit different frequencies of light. The diffraction grating in the camera allows the research team to detect emissions from four elements—iron, calcium, magnesium, and sodium.

The camera, which has been collecting images since March 2016, is just starting to use the diffraction grating, and the team will soon begin collecting spectral data. Information about the chemical composition of meteors is important for scientists to better understand how the planets in our solar system formed.



TESTING NEW TECHNOLOGY TO DIRECTLY IMAGE DISTANT PLANETS

One of the biggest ideas humans have pondered is the possible existence of life elsewhere in the universe. Is the Earth one-of-a-kind, or are there other planets like ours? Are we alone, or does other life exist somewhere else out there?

Scientists have now found conclusive evidence of exoplanets orbiting distant stars, bringing us closer to answering these fundamental questions. Scientists can discover exoplanets by observing the gravitational effects they have on the stars they orbit or by observing the change in starlight when the orbiting planet passes in front of its star. However, Earth-size exoplanets still remain largely invisible to us and cannot yet be studied directly. These exoplanets are billions of times dimmer than their host stars and are incredibly close to the stars, thus imaging them is a significant challenge.

Researchers at the Florida Institute of Technology are aiming to change this by utilizing the ISS National Lab to test a new technology called a **charge injection device (CID)** that will allow scientists to directly image planets around distant stars. For a typical camera, this is difficult because the star is so bright that it saturates the image, washing out the faint light from the planet. The CID, however, does not have this problem due to its design, said principal investigator Daniel Batcheldor, professor at the Florida Institute of Technology.

"It's been very interesting seeing all of these new results coming out about the plurality of worlds around other stars," Batcheldor said. "The CID is a type of sensor that in the future, if mounted on the right type of telescope, will be able to take direct images of distant planets—rather than just seeing the gravitational effects of a planet or the light blocked during a transit, which is what we can do now."

The CID is unique in that it can read light from each pixel independently. This allows the very bright pixels to be read quickly without affecting the pixels around the bright object that are much fainter. This allows researchers to directly image faint objects next to very bright objects within the same frame—such as the faint light of a planet next to a very bright star.

The team tested the CID using a small ground-based telescope at the Florida Institute of Technology, and the results were published in the January 2016 issue of the *Publications of the Astronomical Society of the Pacific*. The team found that the CID imaged several small stars (never before catalogued) around the brightest star in the night sky, Sirius. The faintest of these stars was 70 million times dimmer than Sirius itself. Although these ground-based results are exciting, the ideal location for astronomical observations is not on the ground, but in space, Batcheldor said.

OTHER DIRECT IMAGING METHODS AND ADVANTAGES OF THE CID

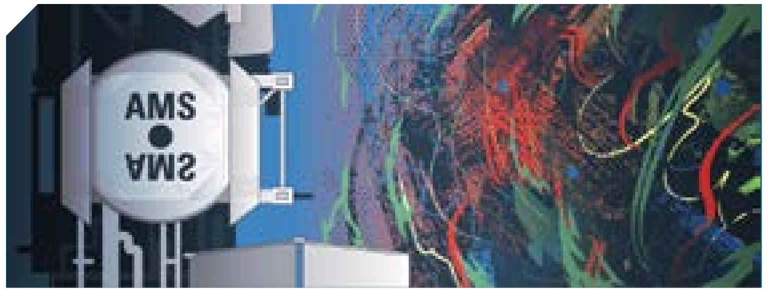
Another way to directly image exoplanets around distant stars is through a method called coronagraphy. This method blocks the direct light from the bright source with a piece of material that is put into the light path of the telescope—much like a driver holding up his hand to block the sun so he can see the much dimmer traffic light, Batcheldor said. However, coronagraphy requires a complex expensive instrument. Also, unlike the CID—which images the full scene—coronagraphy blocks part of the scene, and the image of the bright object is lost.

In the case of imaging a planet around a star, data about the star is vital because the light observed from the planet is a reflection of the starlight. It is important to know if variability in the light from the planet is due to variability in the star's light or due to differences in the reflection of the light from surface features on the planet, such as clouds or oceans.

Thermo Fisher Scientific

To ensure that the technology works as it should in space, the team will be testing the CID onboard the ISS National Lab, and the payload launched to the ISS on SpaceX-10 earlier this month. However, for this mission, the team will not be trying to image planets and stars; instead, the CID will observe a special test pattern inside a box positioned on the NanoRacks external platform outside the ISS. The test pattern is designed to test the extreme contrast ratio ability of the CID. From space, the team expects the CID to achieve a contrast ratio in which the faint object is one billion times fainter than the bright object—the same contrast ratio as between an Earth-like planet and a sun-like star.

The ability to directly image planets around distant stars will help scientists learn more about other planets that may be similar to Earth in size and composition. "The science is massively exciting," Batcheldor said. "An understanding of planets around other stars is going to lead toward the question of whether we are alone in the universe and whether or not there's actually life on some of these other planets."



SEARCHING FOR SIGNS OF DARK MATTER AND PRIMORDIAL ANTIMATTER

The observable universe is about 93 billion light years across and is estimated to contain around two trillion galaxies, but how did it all begin? Is there more to the universe than we can see?

The Big Bang model postulates that the universe began from a tiny, hot, dense point and quickly expanded outward—still expanding today. To better understand the origin and composition of the universe, scientists are asking two key questions: *Is there evidence of primordial antimatter (original antimatter from the early universe) existing somewhere in the universe? And is there evidence of dark matter?*


NASA

Researchers working on AMS-02 are seeking to answer both of these questions. The **Alpha Magnetic Spectrometer** collaboration is searching for evidence of dark matter and primordial antimatter using a large magnet and six particle detectors onboard the ISS National Lab to measure cosmic rays (high-energy particles) passing through our solar system.

AMS-02 is the most sensitive particle detector to ever operate in space, and it allows researchers on Earth to measure the mass, momentum, speed, and charge of particles that pass through the space-based detectors. AMS-02 was launched to the ISS on the Space Shuttle Endeavour in May 2011 and has measured more than 90 billion particles to date.

WHAT IS ANTIMATTER? For each type of matter particle, there is a corresponding antimatter particle. The antimatter particle has the same mass as the matter particle but the opposite charge. For example, a proton has a positive charge, and an antiproton has a negative charge. When matter and antimatter interact, they annihilate into energy.

According to the Big Bang model, there should have been equal amounts of matter and antimatter at the beginning of the universe. In the lab, scientists have detected antimatter particles produced from high-energy collisions of matter particles, but no one has ever detected primordial antimatter.

This has led scientists to the question *Where is all the antimatter left over from the Big Bang?* Because primordial antimatter has never been detected, the current prevailing theory is that there was an imbalance, or asymmetry, of matter and antimatter at the beginning of the universe that resulted in the annihilation of all the antimatter. If evidence of primordial antimatter were found, it would overturn this theory.

AMS-02 is searching for evidence of primordial antimatter by looking for antihelium nuclei. Collisions of particles in space often produce antiprotons and positrons (the antimatter partner of the electron). However, it is highly unlikely that particle collisions would produce an antimatter particle of an element, such as an antihelium nucleus. It is more likely that an antihelium nucleus would be primordial antimatter left over from the Big Bang. For this reason, detection of antihelium nuclei would strongly suggest the existence of primordial antimatter in the universe.

Previous experiments have indicated that if primordial antimatter exists, it is rare, said AMS-02 deputy spokesperson Michael Capell of the Massachusetts Institute of Technology. In order to confirm the existence of primordial antimatter in a statistically significant way, AMS-02 would need to detect not just one or two antihelium nuclei, but several. This would take a long time and would require a lot of data.

> ***"If you examined millions of helium-like cosmic rays, you wouldn't find that one was actually antihelium—so AMS-02 is extending this search to the level of billions," Capell said. "However, even with an experiment as large as AMS-02, it takes years of continuous operations to collect these billions of cosmic rays, and each must be examined in detail to figure out if it is or is not antihelium."***

WHAT IS DARK MATTER? Dark matter, an invisible form of matter that does not reflect, absorb, or emit light, is believed to be prevalent in the universe. Scientists postulate dark matter exists because of a gravitational effect observed in galaxies.

As a galaxy rotates, gravity holds together all of the matter in the galaxy, keeping it from being flung apart as it spins. However, scientists have found that galaxies appear to be rotating at speeds faster than they should be based on the amount of matter that can be observed in the galaxies. In other words, the amount of matter that can be observed in the galaxies does not provide enough mass for gravity to be able to hold the galaxies together at the speeds at which they are rotating.

NASA

The fact that galaxies are not being flung apart led scientists to believe that there must be some form of invisible matter that we cannot directly detect that is providing more mass, and thus more gravity to hold the galaxies together. Scientists termed this invisible matter "dark matter." Because dark matter cannot be directly detected, AMS-02 is looking for evidence of dark matter interactions with matter or other dark matter.

The AMS-02 collaboration has had eight major papers published in *Physical Review Letters* and has repeatedly made measurements that existing theories cannot explain—redefining high energy physics. Several AMS-02 results hint at the existence of dark matter; however, more data is needed to confirm evidence of its existence.

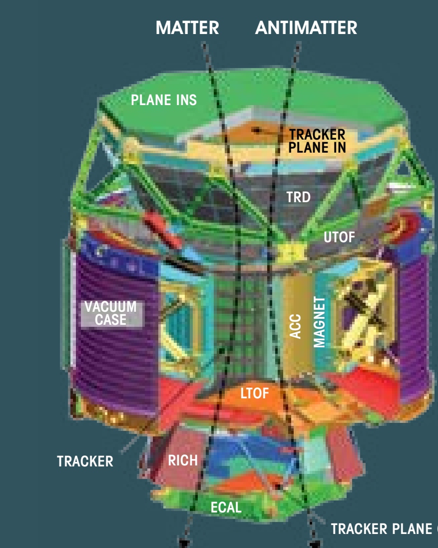
> *"While the AMS-02 measurements hint at the existence and nature of dark matter, we can't yet pin it down," Capell said. "However, if the AMS-02 measurements continue the trend they have shown so far, we should be able to determine the mass of dark matter."*

By utilizing the ISS National Lab to look outward into space, we are learning more about the universe around us. We can study meteors to get a glimpse of what our early solar system was like, we can use new technology to directly image distant Earth-like exoplanets that could potentially harbor life, and we can use cutting-edge particle detectors to gain a better understanding of the origin and composition of our universe. ■

MEASURING COSMIC RAYS FROM SPACE

The AMS-02 experiment must be done from space because Earth's atmosphere and magnetic field shields us from cosmic rays—the charged particles that the detectors need to measure. This makes it impossible to conduct the experiment from the ground.

Because AMS-02 has six detectors, the same particle can often be measured by several different detectors, allowing the research collaboration to cross-check results. AMS-02 is able to make measurements to an accuracy of 1%—by comparison, most other space-based detectors are only able to measure to an accuracy of 30%.



AMS – A TeV Precision, Multipurpose Spectrometer

Scientist Astronaut Leads Research in Space for Life on Earth

BY LIZ WARREN

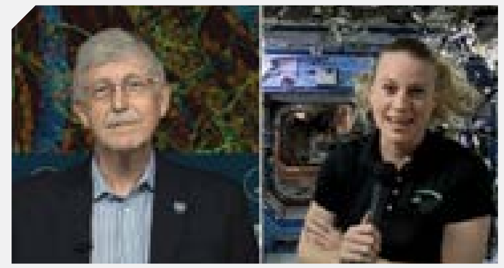
While NASA Astronaut Kate Rubins was onboard the ISS, she operated hundreds of experiments, ventured outside the space station for two spacewalks, and welcomed three cargo spacecraft delivering tons of supplies. She also had the opportunity to speak with Francis Collins, director of the National Institutes of Health, live from the ISS during a downlink last October.

"I actually applied to become an astronaut while procrastinating a little bit on writing an R01 grant (NIH research program grant) application," Rubins told Collins during the downlink. Selected by NASA in 2009, Rubins has a Ph.D. in cancer biology from Stanford University Medical School.

Rubins and Collins discussed utilizing the unique environment of space to study diseases that affect people on Earth. NIH, NASA, and CASIS have long-standing collaborations aimed at investigating human health in the space environment. Microgravity and radiation have profound effects on cells, tissues, organs, and whole-system biology that can advance our understanding of aging, cancer, and other medical conditions. Toward this end, NIH has sponsored several investigations onboard the ISS National Lab in recent years, and more collaborations are underway—including a recent funding opportunity for tissue chips in space that have promise to advance human health on Earth.

In addition to discussing general biomedical research in microgravity, Rubins and Collins also talked about DNA, the hereditary material found in every living cell. Fourteen years ago, Collins led the Human Genome Project as it completed its historic mapping of the entire human genome sequence. At the time of the downlink, Rubins had recently become the first person to sequence DNA in space—an achievement Collins also highlighted after the downlink, in his NIH Director's Blog about 2016 research.

The DNA sequencing effort was both an experiment and a technology demonstration, Rubins said. It was uncertain whether DNA sequencing would work in space because fluids behave differently in microgravity, and any bubbles in the system could be problematic. However, Rubins was able to show that DNA sequencing in space could successfully be done using a hand-held, off-the-shelf device called MinION. The MinION sequencer and other molecular biology facilities onboard the space station allow for *in situ* analysis of samples rather than having to return samples to Earth.



NIH Director Francis Collins spoke with NASA Astronaut Kate Rubins about ISS research during a downlink on October 18, 2016. NASA

With recent advances in systems biology, high throughput analytics, cutting-edge technologies, and access to a well-equipped orbiting laboratory, this is an exciting time for researchers. Collins said, "If you have a passion to make a discovery, to make a difference in the world, to add to the knowledge of the universe, science is a great place to be right now."

Inspiring Students through Amateur Radio on the ISS

BY DAN BARSTOW

In 2000, amateur radio operators conducted the first amateur radio contact between an operator on the ground and a crew member onboard the ISS. This was the start of the ARISS (Amateur Radio on the ISS) program, a unique educational program that provides students worldwide in grades K-12 with the opportunity to participate in amateur radio communication with crew members onboard the ISS. ARISS conducted its 1,000th student contact with the ISS last year, and the program has become a robust pathway for students and the public to directly engage with ISS crew members.

To prepare for an ARISS contact, students work with local amateur radio operators to set up a ground-based amateur radio station at their school. A typical contact lasts around 10 minutes (the amount of time the ISS takes to pass overhead). The excitement of the event often draws a large local audience in addition to the students participating in the contact.

Students experiment with radio and wireless technology, an interest that developed after their school participated in the ARISS program. Matt Severin, Dowagiac Middle School principal

Students prepare for the contact by learning how to use the orbit prediction program and how to track the ISS during the contact. They also help assemble the transmitting station and brainstorm creative questions to ask crew members during the contact. Students have asked crew members questions like, "How do you decide which experiments to take into space?", "What do you do to get ready for a spacewalk?", "What does your spacesuit do for you and what would happen without it?", and "How can I become an astronaut?".

Through the ARISS program, students have the opportunity to learn about several science, technology, engineering, and mathematics (STEM) topics, including orbital mechanics, space science, radio science, electronics, wireless technology, and amateur radio operation. In addition to preparing for the contact, students and teachers often do extensive follow-up activities on related STEM topics.

"ARISS has a bold goal," said ARISS director Frank Bauer (ham call sign KA3HDO), who is also one of the founders of the ARISS program. "We want to use the wonder of the space station and the power of amateur radio communications to inspire kids to pursue STEM fields." ARISS also has scientific and engineering goals—to experiment with new technologies and alternative pathways of communication with the ISS.

The ARISS U.S. program is managed by the Radio Amateur Satellite Corporation North America (AMSAT-NA), the American Radio Relay League, and NASA. CASIS is a funding sponsor for ARISS and provides access to ISS crew members (who are also licensed amateur radio operators), radio equipment onboard the ISS National Lab, and connection to the Space Station Explorers network of STEM educational programming (www.spacestationexplorers.org).

Any school can apply to host a contact, and all contacts require careful coordination to confirm the pass-over timing and availability of ISS crew members. ARISS also coordinates with local volunteers from the amateur radio community around the school who provide support for the contact.

ARISS reaches more than 15,000 students per year, as well as a broader community audience of more than 12 million per year who have witnessed a contact in person or through the media. Each contact is an unforgettable experience for the students and others who participate.

"The ARISS project has become one of the most engaging and far-reaching educational programs on the ISS National Lab," said CASIS Director of Operations and Education Ken Shields. "ARISS is the perfect embodiment of ISS education, connecting students directly with crew members on the ISS, and we are extremely proud to have ARISS as a Space Station Explorers STEM education partner."

To learn more about ARISS and how students can speak to ISS crew members in space, please visit *www.ariss.org*.

Investing in Innovation: Launching Start-ups with ISS Research

BY PATRICK O'NEILL

Early-stage entrepreneurs are major drivers of innovation and not only contribute to the U.S. economy but create new markets for the world. Over the past four years, CASIS has partnered with the Boston-based organization MassChallenge (through their business accelerator program) to help fund start-up companies that have unique and innovative concepts that could be enhanced through research onboard the ISS National Lab. This is the third year that CASIS has partnered with the Boeing Company for the competition, and CASIS and Boeing have collectively awarded $1.5 million in seed funding and hardware development costs to eight companies through MassChallenge.

In November 2016, CASIS and Boeing awarded financial support to three new companies through MassChallenge, highlighted here.

ANGIEX, INC. • ***Endothelial Cells in Microgravity as a Model System for Evaluation of Cancer Therapy Toxicity***

Angiex, Inc., a biotechnology company based in Cambridge, Massachusetts, is working to develop a new type of cancer therapy with broad application to different cancers. Although there are many different types of cancers, all solid tumors must generate new blood vessels to grow. Angiex has created a novel cancer therapy that targets a protein involved in the proliferation of the cells that line the walls of blood vessels—called endothelial cells (ECs). Angiex will evaluate the hypothesis that microgravity-cultured ECs represent a valid model system to test the effects of vascular-targeted drugs on normal blood vessels. If the hypothesis is validated, microgravity-cultured ECs would constitute an important model system for evaluating the action of any vascular-targeted drug.

DOVER LIFESCIENCES • ***Microgravity Crystallization of Glycogen Synthase-Glycogenin Protein Complex***

Dover Lifesciences, a biotechnology company based in Dover, Massachusetts, is working to develop new drugs for metabolic diseases. The crystallization of proteins for structural determination is an important tool for drug discovery. Dover Lifesciences aims to utilize the microgravity environment on the ISS to crystallize a medically relevant protein complex that has not been crystallized on Earth with adequate uniformity to enable high-resolution structural analysis. Determination of the structure of this protein complex may aid in the development of drugs that could be used to treat obesity, rare genetic disorders, and potentially cancer.

LAMBDAVISION, INC. • ***Enhancement of Performance and Stability of a Protein-Based Retinal Implant by Manufacturing in Microgravity***

LambdaVision, Inc., a biotechnology company based in Farmington, Connecticut, is working to develop a protein-based retinal implant to restore vision to the millions of people with blindness resulting from degenerative eye diseases. The retinal implant is generated utilizing an automated approach to deposit multiple layers of a light-sensitive protein, bacteriorhodopsin, into a flexible architecture. Gravity interferes with the homogeneity and uniformity of the layers during deposition, and LambdaVision hypothesizes that preparing the multi-layer films in microgravity will improve the homogeneity of the film layers, the orientation of the protein within the film, and the stability of the resulting multilayer system.

The mission of the ISS National Lab is to provide access and opportunity for research that uniquely leverages the microgravity environment of the ISS to benefit life on Earth. The next great discovery or innovation for our planet may come from research conducted off our planet, and investment in innovative ideas from start-up companies could yield returns capable of changing the way that we live.

The Role of the ISS National Lab in Regenerative Medicine Research

BY JANA STOUDEMIRE

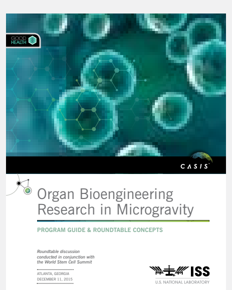
Advances in stem cell biology, the development of tissue chips, and 3D bioprinting on Earth are helping to accelerate drug discovery and bring the possibility of bioengineering whole organs for transplantation closer to reality. These advances in regenerative medicine are being further accelerated using the ISS National Lab—a one-of-a-kind environment available to physicians, researchers, and technology developers.

In space, several changes take place in cells, including changes in cell signaling (the way cells share information) and cell aggregation (the physical contact between cells leading to their 3D structural organization into tissues). Microgravity also profoundly changes the physics of fluid movement and the expression of genes in cells. These cellular changes provide opportunities for discoveries that cannot be made on Earth.

Tissue culture bottles. NASA

In addition, the effects of microgravity on genes, cells, and organisms sometimes result in changes that mimic and accelerate the onset and progression of diseases seen on Earth. Thus, the ISS provides a platform to develop models to better study diseases (such as those affecting the heart, immune system, bones, and muscles) and therapies aimed at prevention and treatment.

In a project launched to the ISS on SpaceX CRS-9 in July 2016, researchers from Stanford University turned stem cells into beating heart cells for the first time in space—an accomplishment that NASA Astronaut Kate Rubins described as a moment in her time onboard the space station that took her breath away, like looking back at the Earth from space for the first time. The beating of heart cells in space is a significant milestone in medical research, but it is just the beginning of R&D on the ISS National Lab that will provide new insights in the field of regenerative medicine.



CASIS Report on Organ Bioengineering in Microgravity, released 2016

A stem cell experiment focused on the development of stroke therapies, conducted by researchers at the Mayo Clinic, was sent to the ISS National Lab on SpaceX CRS-10, which launched earlier this month. An additional stem cell investigation aimed at the development of therapies for heart disease, conducted by researchers at Loma Linda University, is expected to launch to the ISS on SpaceX CRS-11 later this year. Researchers at Houston Methodist are also working to prepare an investigation that will utilize microgravity to help develop 3D models of lung tissue.

Last year, CASIS issued a "3D Microphysiological Systems for Organs-On-Chips Grand Challenge." The competition's winning teams, from Micro-gRx and the University of Pittsburgh, are now preparing flight experiments that will help develop 3D models to observe muscle and bone cell organization into tissues in order to study musculoskeletal disorders and evaluate potential therapies for prevention and treatment. CASIS is also working with AxoSim Technologies to further develop nerve-on-a-chip models to study how nerve cells (and the sheath that protects them) form into functioning neural systems.

Advancing stem cell therapies and developing 3D tissue models are the first steps toward understanding how to create tissues and eventually whole organs for transplantation.

A significant hurdle to creating thick tissues is the ability to generate a vascular network that allows nutrients to diffuse through the thick cell layers that form human tissues—a challenge that CASIS, together with NASA, is working to address.

Through the NASA Centennial Challenges Program "Vascular Tissue Challenge," teams seek to create thick, human vascularized tissues in competition for a $500,000 prize purse. Additionally, CASIS partnered with the New Organ Alliance and the Methuselah Foundation to offer one winning team selected from the Vascular Tissue Challenge the opportunity to launch an experiment to the ISS National Lab to demonstrate their technology for tissue vascularization in space. The CASIS Innovations in Space Award will provide $200,000 for flight hardware and support for the team to advance research on thick-tissue vascularization in the unique environment of microgravity.

"Results from research conducted in microgravity have the potential to advance the field of regenerative medicine and bring us closer to the goal of bioengineering full organs and advanced tissue constructs that may help to end the organ shortage," said Joshua Neubert, who leads the New Organ Alliance. "These awards are a first step in supporting exciting new areas of bioengineering innovation." ■

SPOT LIGHT

News & Notes

FROM THE ISS NATIONAL LAB

FUNDING OPPORTUNITY

In November, CASIS and the National Science Foundation (NSF) announced a joint solicitation for researchers to submit proposals to study fundamental combustion science and thermal transport onboard the ISS National Lab—up to $1.8 million will be awarded for multiple research investigations. All proposals must demonstrate a tangible benefit to improving life on Earth. For more information about this funding opportunity, view the full NSF proposal solicitation at www.spacestationresearch.com/nsf-combustion.

CASIS ANNUAL REPORT

In January, CASIS released the 2016 Annual Report in its new online format. The new interactive, mobile-friendly format summarizes key achievements of the ISS National Lab, demonstrating continued success, engagement and investment from new user communities, enabling commercialization, and targeted outreach. The report also features links to in-depth information on research projects in the pipeline, current metrics and resources, and an interactive map of the ISS National Lab Network. To explore the 2016 CASIS Annual Report, go to ar2016.iss-casis.org.

ON THE ROAD

CASIS is hitting the road to meet with researchers, students, and the aerospace community. CASIS attended the 2017 AAAS Annual Meeting in Boston and hopes to catch you at the National Science Teachers Association's National Conference in Los Angeles in March and the National Space Symposium in Colorado Springs in April.

LAUNCHING TO THE ISS

SpaceX CRS-10 launched earlier this month, carrying a variety of payloads to the ISS National Lab, and an Orbital ATK resupply mission is anticipated in early spring. Key payloads on these missions include projects involving rodent research, protein crystallization, cell biology, technology development, and materials science.